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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/491,896	01/24/00	DURING	M 102194-6

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EXAMINER	
BUNNER, B	
ART UNIT	**PAPER NUMBER**
1647	9

DATE MAILED: 02/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/491,896	DURING, MATTHEW J.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 December 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-85* is/are pending in the application.

4a) Of the above claim(s) *4,13-21,33-35,47-53,55-58,62-67,69 and 77-85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-12, 22-32, 36-46, 54, 59-61, 68, and 70-76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claims *1-85* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5 .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☒ Other: *Substitute PTO-948* .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group I, (claims 1-12, 22, 25-32, 36, 38-44, 54, 56-68) drawn to method of treatment of a subject with a neurological disease consisting of administering an amino acid vaccine in Paper No. 8 (06 December 2000) is acknowledged. Applicant's election with traverse of epilepsy as the species of neurological disorder and neuroreceptors as the species of antigen target protein in Paper No. 8 (6 December 2000) is acknowledged. The traversal is on the ground(s) that the invention of the instant application has a unifying concept of using circulating antibodies that are effective against targets in the nervous system and therefore, the claims of Groups I, II, and III should not be separated into different inventions. Applicant states that antibodies are generated by either an antigen that elicits the production of antibodies or is a composition comprising antibodies. The invention is not how the antibodies are produced, but rather how the circulating antibodies are used to treat a neurological disorder. This is not found persuasive because the methods of Groups I , II, and III require different ingredients. For example, the method of Invention I requires search and consideration of administration of a NMDAR1 protein, which is composed of amino acids. The method of Invention II requires search and consideration of administration of NMDAR1 DNA, which is composed of nucleic acids. The method of Invention III requires search and consideration of administration of an antibody or antibody fragment against NMDAR1. The requirement is still deemed proper and is therefore made FINAL.

Upon further consideration, claims 23-24, 37, 45-46, 71, and 75-76 (from Groups III and IV) of the restriction in Paper No. 6 (07 September 2000) have been rejoined. These claims are under examination only with respect to the election of the invention of Group I.

Claims 62-67 were restricted to separate groups (Group II, III) in the previous restriction (Paper No. 6, 07 September 2000) and were unintentionally included in Group I by the Examiner. Therefore, claims 62-67 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 4, 13-21, 33-35, 47-53, 55-58, 62-67, 69, 77-85 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8 (06 December 2000).

Claims 1-3, 5-12, 22-32, 36-46, 54, 59-61, 68, and 70-76 are under examination in the instant application.

Drawings

1. The drawings are objected to because they are of insufficient quality to permit analysis. Applicant is required to provide new informal drawings of better quality.

Specification

2. The abstract of the disclosure is objected to because a "." is missing in line 5 before the term "Animal". Correction is required. See MPEP § 608.01(b).

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "NMDAR1 vaccine for the treatment of epilepsy".

4. The disclosure is objected to because of the following informalities:

4a. The use of the trademarks NEUROBASAL (pg 47, line 1), MINI COMPLETE (pg 49, line 26) have been noted in this application. They should be capitalized wherever they appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

4b. The Brief Description of Drawings refers to Figures 2A-2H, but there is no description of Figures 2E-2H.

4c. The Brief Description of Drawings refers to a bar chart in Figure 6H, but the bars in Drawing 6H are not labeled and it cannot be determined which bars represent which animals.

4d. The Brief Description of Drawings refers to two line graphs in Figures 7A-7B, but the various lines which represent different animal groups in Drawings 7A-7B cannot be differentiated between one another. The Description refers to one line being dashed and one line being solid, but both lines are solid.

4e. The Brief Description of Drawings refers to different rat groups in Figures 12A-12D, but it cannot be determined which lines and bars represent each particular rat group in Drawings 12A-12D.

Appropriate correction is required.

Claim Objections

5. Claim 3 is objected to because of the following informalities:

5a. The word "disease" should be inserted after both "Alzheimer's" and "Parkinson's" in line 2 of the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-3, 5-12, 22-32, 36-46, 54, 59-61, 68, and 70-76 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 1-3, 5-12, 22-32, 36-46, 54, 59-61, and 68 recite a method for treating a subject with epilepsy or at risk of developing epilepsy, a method for treating a neuroendocrine disorder, a method for modifying the function of a target neuroreceptor, and a method for improving cognition comprising administering an amino acid vaccine comprising a therapeutically effective amount of the antigen, NMDAR1, wherein the antigen elicits the production of antibodies. Claims 70-76 recite a pharmaceutical composition comprising a therapeutically effective amount of the antigen, NMDAR1, wherein the antigen elicits the production of antibodies.

The specification proposes methods for treating neurological and neuroendocrine disorders, for modifying the function of a target protein in the central nervous system, and for improving cognition comprising administering an antigen (protein) vaccine. In regards to the elected invention of the instant application, the specification defines an "antigen" as "a substance or a material that is specifically recognized by an antibody and to which an antibody can be

generated" (pg 14, lines 4-6). However, the specification does not teach effective antigen administration, such as quantity or route of administration, to achieve the desired production of antibodies. Further, the working examples with the genetic vaccine do not provide guidance regarding how to administer the protein vaccine. The specification does not disclose any methods or working examples directed to the treatment neurological and endocrine disorders with the antigen vaccine. The specification provides no guidance or working examples directed to the modification of the function of a target protein or to the improvement of cognition with the antigen vaccine.

The specification also does not teach one skilled in the art how to use a "pharmaceutical" composition comprising the NMDAR1 antigen without undue experimentation for the treatment of a disease in a subject. The specification lists disorders to be treated (pg 3, lines 9-12), but there are no working examples directed to a particular disorder in an animal or administration of the NMDAR1 antigen to an animal. (Note, this issue could be overcome by deleting the word "pharmaceutical" from the claims.)

The state of the art is such that numerous problems exist in regards to administering a subunit (antigen) vaccine to humans and animals. Several characteristics of an ideal vaccine, regardless of species, must include: 1) efficacy greater than 90%, 2) effective after a single dose, 3) long lived immunity, 4) effective when given orally, and 5) high safety (Babiuk, LA. *Vaccine 17*: 1587-1595, 1999). Often, when some proteins are included in a vaccine, they may be immunosuppressive, but in other cases, the immune responses to proteins may enhance the disease (Babiuk, pg 1588, col 2). Although antigen vaccines have the advantage of increased safety, their major disadvantages are their low level of immunogenicity and rapid degradation *in*

vivo. The rapid degradation *in vivo* may explain the low immunogenicity, even if linked to a carrier or strong adjuvant (pg 1588, col 2; pg 1590, col 2).

Due to the large quantity of experimentation necessary to determine the most effective administration of the antigen vaccine and antigen pharmaceutical composition, the lack of direction/guidance presented in the specification regarding administration of the antigen vaccine and the treatment of neurological and neuroendocrine disorders and modification of the function of a target protein with the antigen vaccine, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of the response and longevity of the antigen vaccine and antigen pharmaceutical composition *in vivo* (see discussion and recited reference), undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-3, 5-12, 22-32, 36-46, 54, 59-61, 68, 73-74, and 76 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7a. Claims 1-3, 5-12, 22-32, 36-46, 54, 59-61, and 68 are indefinite because the claims do not have a step that clearly relates back to the preamble.

7b. Regarding claims 7, 26-27, 39, 46, 73, and 76 the acronym "NMDA" renders the claims vague and indefinite. Abbreviations should be spelled out in all independent claims for clarity.

7c. Regarding claims 8, 28, 40, and 74 the acronym "NMDAR1" renders the claims vague and indefinite. Abbreviations should be spelled out in all independent claims for clarity.

7d. Regarding claim 26 the acronyms "GluR", "NPY", and "NK-1" render the claim vague and indefinite. Abbreviations should be spelled out in all independent claims for clarity.

7e. Regarding claims 9, 29, 41, and 59, the phrase "or a combination thereof" renders the claims vague and indefinite because it is unclear what particular combinations of vaccines are recited.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 7:30-4:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

Bridget E. Bunner
Art Unit 1647
February 7, 2001

ELIZABETH KEMMERER
PRIMARY EXAMINER